REMARKS

Claims 23-54 are currently pending on entry of the amendments above.

Claims 1-22 have been cancelled without prejudice or disclaimer and Applicants reserve the right to pursue the subject matter of these claims in related applications.

New claims 23-54 have been added. Support for these claims is found throughout the specification and claims as originally filed. Specifically, such support may be found, for example, at page 6, ¶32 as well as in Figure 3; at page 13, ¶69; at page 18, ¶97; at page 19, ¶¶99 and 101; at page 20, ¶¶106-108; at page 21, ¶¶110-111; at page 29, ¶146; and at page 30, ¶155. Accordingly, no new matter has been introduced.

I Restriction Requirement

The Examiner has required an election under 35 U.S.C. § 121 of one of the following groups:

I. Claims 1-11, drawn to a polynucleotide encoding SEQ ID NO:2, a vector, a host cell, and a method for producing a polypeptide of SEQ ID NO:2, classified in class 435, subclass 69.1.

II Claims 12-13, drawn to a polypeptide of SEQ ID NO:2, classified in class 530, subclass 350.

III Claim 14, drawn to an agonist of SEQ ID NO:2, classified in class 530, subclass 300, as exemplified in the Specification at 38, ¶ 195.

IV Claim 15, drawn to an antibody to SEQ ID NO:2, classified in class 530, subclass 387.1.

V Claim 16, drawn to an antagonist, classified in class 530, subclass 387.1, as exemplified in the Specification at 38, ¶ 195.

VI Claims 17-19, drawn to a method for treatment with SEQ ID NO:2, classified in class 514, subclass 2.

VII. Claims 20-21, drawn to a method for diagnosing a disease, classified in class 435, subclass 7.1.

VIII. Claim 22, drawn to a method of compound identification, classified in class 435, subclass 7.2.

See, Paper No. 02052004, pages 2-5. The Examiner contends that the inventions are distinct, each from the other.

As indicated by the Examiner, during a telephone conversation on January 30, 2004, Attorney for Applicants made a provisional election without traverse of the subject matter of group II, drawn to polypeptides of SEQ ID NO:2, corresponding to original claims 12 and 13, for further prosecution.

Applicants point out that claims 1 to 22 have been canceled and that new claims 23 to 54 are directed to subject matter falling within the ambit of group II as cast by the Examiner.

II Rejections Under 35 U.S.C. §§ 101 and 112, first paragraph

a. Non-statutory subject matter

The Examiner has rejected claims 12 and 13 under 35 U.S.C. § 101, as allegedly being directed to non-statutory subject matter. More specifically, the Examiner alleges that "[t]he claims are directed to polypeptides, but do not contain the limitation wherein the polypeptide is isolated, and thus the claims read on a product of nature." *See*, Paper No. 02052004, at page 6.

Applicants respectfully point out that claims 12 and 13 have been cancelled without prejudice or disclaimer, thereby obviating the present rejection. Accordingly, Applicants respectfully request that the Examiner reconsider and withdraw the present rejection under 35 U.S.C. § 101.

b. Patentable utility

The Examiner has further rejected claims 12 and 13 under 35 U.S.C. § 101, as allegedly having no apparent or disclosed patentable utility. More specifically, the Examiner alleges:

> [t]he instant application does not disclose the biological role of this protein or its significance ... the nucleic acid

> encoding the CCIII polypeptide has been isolated because of its similarity to known proteins, as set forth in the Specification at 14, ¶73. However, it is commonly known in the art that sequence-to-function methods of assigning protein function are prone to errors ... [a]fter complete characterization, this protein may be found to have a patentable utility ... [u]ntil some actual and specific significance can be attributed to the protein identified in the specification as CCIII, the instant invention is incomplete.

See, Paper No. 02052004, at pages 6-8. Applicants respectfully disagree and traverse this rejection.

Applicants respectfully point out that claims 12 and 13 have been cancelled without prejudice or disclaimer, thereby obviating the present rejection. However, Applicants will address this rejection as it pertains to pending claims 23-54.

A rejection under 35 U.S.C. § 101 is improper when a person of ordinary skill in the art would find credible disclosed features or characteristics of the invention, or statements made by the Applicants in the written description of the invention. *See* M.P.E.P. §§ 2107.01(II), (III) at 2100-[33-36] (Rev. 1, Feb. 2003). In addition, Applicants need only make *one* credible assertion of utility for the claimed invention to satisfy 35 U.S.C. § 101. *See, e.g., Raytheon v. Roper,* 724 F.2d 951, 958, 220 U.S.P.Q. 592, 598 (Fed. Cir. 1983), *cert. denied,* 469 U.S. 835 (1984) ("When a properly claimed invention meets at least one stated objective, utility under 35 U.S.C. § 101 is clearly shown."). *See*, M.P.E.P. at 2100-33. Finding a lack of utility is also improper if a person of ordinary skill in the art would know of a use for the claimed invention at the time the application was filed. M.P.E.P. § 2107.01(II)(B) at 2100-[33-34].

Moreover, the burden is on the Examiner to establish why it is more likely than not that one of ordinary skill in the art would doubt *(i.e.,* "question") the truth of the statement of utility. M.P.E.P. § 2107.01(II) at 2100-[33-34]. Thus, the Examiner must provide evidence sufficient to show that the statement of asserted utility would be considered

"false" by a person of ordinary skill in the art. *Id.* The Examiner must also present countervailing facts and reasoning sufficient to establish that a person of ordinary skill would not believe the applicants' assertion of utility. *See id.*; *see also, In re Brana,* 51 F.3d 1560, 34 U.S.P.Q.2d 1436 (Fed. Cir. 1995). For the reasons set forth below, the Examiner has not met the burden that is necessary to establish and maintain a rejection for lack of utility under 35 U.S.C. § 101.

Contrary to the Examiner's comments, Applicants have set forth in the specification, a specific, substantial and credible utility which supports the claimed polypeptides of the present invention. In the specification at page 31, ¶157, Applicants teach that the invention is useful as a diagnostic reagent, for example, in the "diagnosis of a disease or susceptibility to a disease which results from under-expression over-expression or altered expression of CCIII, for example, neoplasia such as cancers and tumors." Therefore, Applicants submit that the specification clearly and specifically asserts a use for the claimed invention, *i.e.*, the diagnosis of cancers and tumors. The asserted utility for the claimed polynucleotides of the present invention is supported by post filing date references to which the Examiner's attention is respectfully directed, and which are attached hereto as Exhibit A (Chien, W. and Pei, L. (2000) *J. Biol. Chem.* 275(25): 19422-19427), and Exhibit B (McCabe, C.J., *et al.* (2003) *Clin. Endocrinol.* 58(2): 141-150).

Chien and Pei (Exhibit A) disclose a polynucleotide which encodes the CCIII polypeptide of the present invention and identify this polynucleotide as "PTTG binding factor (PBF)". *See*, Exhibit A, page 19423. Chien and Pei demonstrate that "PBF" binds directly to Pituitary tumor-transforming gene (PTTG), a polypeptide believed responsible for tumorigenesis in the pituitary and various other tissues. *See*, Exhibit A, page 19422, and Figures 3-5 at pages 19423-19424. Chien and Pei further demonstrated that "PBF" binding is required for PTTG activation of transcription from the bFGF promoter. *See*,

Exhibit A, Figure 9 at page 19426. The authors finally conclude that PBF binding to PTTG "suggest a potential mechanism by which PTTG might function as a transcriptional activator." *See*, Exhibit A, page 19427. Because the polypeptide identified by Chien and Pei as "PBF" is identical to CCIII of the present invention, and because the polypeptide identified by Chien and Pei as "PBF" is specifically required for the transcriptional activation activity of a known oncogene, the observations described above confirm Applicants' assertion of a specific utility that the CCIII polypeptides, antibodies and polynucleotides of the present invention will be useful in the diagnosis of cancers and tumors.

Furthermore, McCabe et al. (Exhibit B) demonstrate that expression of "PBF" was upregulated sixfold in pituitary tumors isolated from a large cohort of patients. See, Exhibit B at page 144, right column first paragraph; and page 145, Figure 2. McCabe et al. determine "[o]ur data support a fundamental role for PTTG-mediated upregulation of FGF-2 signalling in pituitary tumorigenesis." See, Exhibit A at page 141, right column lines 7-9. Because the polypeptide identified by McCabe et al. as "PBF" is identical to CCIII of the present invention, because the polypeptide identified by McCabe et al. as "PBF" is upregulated in pituitary tumors, and because the polypeptide identified by McCabe et al. as "PBF" is required for PTTG activation of FGF transcription, the observations described above confirm Applicants' assertion of a specific utility that the CCIII polypeptides, antibodies and polynucleotides of the present invention will be useful in the diagnosis of cancers and tumors.

Thus, polynucleotides of the invention, together with polypeptides which they encode and antibodies specific for those polypeptides, may be used in the diagnosis of cancers such as, for example, pituitary cancer (*See*, *e.g.*, Specification at page 31, ¶157; and at page 34, ¶171). Applicants submit that, for example, the use of polypeptides,

antibodies, or polynucleotides of the invention, in the detection of pituitary cancer, is a specific utility in that detection of this disorder is not possible with all polypeptides. This utility is also substantial in that improved detection of this disorder would substantially benefit patients and their healthcare providers throughout the world.

In light of the above facts, Applicants submit that one of ordinary skill in the art would have found the Applicants' asserted utility to be more likely than not true, and therefore the Applicants asserted utility is credible. Therefore, Applicants argue that the present invention meets the statutory utility requirement under 35 U.S.C. § 101, and as further described in the Utility Examination Guidelines, Federal Register, Vol. 66, No. 4, pages 1092-1099, Friday January 5, 2001.

Other than the conclusory statements that the invention lacks utility, the Examiner has presented no arguments as to why Applicants' asserted utility is not credible. In arguing that Applicants' asserted utility is not credible, the Examiner must attack (a) the logic underlying the assertion as seriously flawed or (b) the facts upon which the assertion is based as inconsistent with the logic underlying the assertion. *See*, Revised Interim Utility Guidelines Training Materials, p. 5. In the instant rejection, the Examiner has set forth no arguments as to why Applicants' logic (that human CCIII may be used in the detection and/or diagnosis of cancers and tumors) is flawed or that the facts upon which the logic is based on, are inconsistent with the underlying assertion. Thus, the Examiner has failed to make even a *prima facie* showing that Applicants' asserted utility is not credible.

Applicants submit that the asserted utilities for human CCIII are specific and substantial ("the general rule [is] that the treatments of specific diseases or conditions meet the criteria of 35 U.S.C. § 101." (Revised Interim Utility Guidelines Training Materials, p. 6)). In addition, Applicants submit that these utilities are credible. The Examiner has

failed, however, to provide any countervailing statements as to why these particular utilities are not specific, substantial and credible.

Even assuming, *arguendo,* the Examiner has established a *prima facie* showing that the claimed invention lacks utility, Applicants respectfully submit that they have rebutted the Examiner's showing by proffering sufficient evidence to lead one skilled in the art to conclude that the asserted utilities are more likely than not true. Applicants have directed the Examiner to the specification where clear and specific assertions are made in support of patentable utilities of human CCIII and sequences of the present invention.

In view of the above, Applicants submit that the asserted utilities of the invention meet the statutory requirement set forth in 35 U.S.C. § 101. Accordingly, Applicants respectfully request that the rejection be withdrawn.

The Examiner also rejects claims 12 and 13 under 35 U.S.C. § 112, first paragraph. Specifically, it is the Examiner's contention that claims 12 and 13 are "not supported by either a specific and substantial asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention." *See*, Paper No. 02052004, at page 9. Applicants respectfully disagree and traverse this rejection.

Again, Applicants respectfully point out that claims 12 and 13 have been cancelled without prejudice or disclaimer, thereby obviating the present rejection. However, Applicants will address this rejection as it pertains to pending claims 23-54.

For the reasons discussed above in response to the rejection under 35 U.S.C. § 101, Applicants respectfully assert that the claimed invention is supported by a specific and substantial asserted utility. The Examiner "should not impose a 35 U.S.C. § 112, first paragraph, rejection grounded on a 'lack of utility' basis unless a 35 U.S.C. § 101 rejection is proper." M.P.E.P. § 2107.01 (IV) at 2100-[36-37]. Therefore, because the claimed

invention complies with the utility requirement of 35 U.S.C. § 101, Applicants respectfully request that the Examiner reconsider and withdraw the rejection under 35 U.S.C. § 112, first paragraph, based on the alleged lack of utility of the claimed invention.

c. Enablement

The Examiner has further rejected claims 12 and 13 under 35 U.S.C. § 112, first paragraph, as allegedly failing to "enable any person skilled on the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims." More specifically, the Examiner alleges:

> [t]he claims encompass variant polypeptides, and claims 12 and 13 are overly broad since insufficient guidance is provided as to which of the myriad of variant polypeptides which (*sic*) will retain the characteristics of CCIII ... Applicants do not disclose any actual or prophetic examples on expected performance parameters of any of the possible muteins of human CCIII ... given the art recognized unpredictability of the effect of mutations on protein function, it would require undue experimentation to make and use the claimed invention.

See, Paper No. 02052004, at pages 9-11. Applicants respectfully disagree and traverse this rejection.

Again, Applicants respectfully point out that claims 12 and 13 have been cancelled without prejudice or disclaimer, thereby obviating the present rejection.

Applicants further respectfully point out that pending claims 23-54 do not encompass variant polypeptides. Accordingly, Applicants respectfully request that the Examiner reconsider and withdraw the present rejection under 35 U.S.C. § 112, first paragraph, for lack of enablement.

d. Written description

The Examiner has further rejected claims 12 and 13 under 35 U.S.C. § 112, first paragraph, as allegedly "containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention." More specifically, the Examiner alleges:

> [t]hese are genus claims because the claims encompass variant polypeptides ... [s]ince the disclosure fails to describe the common attributes or characteristics that identify members of the genus, and because the genus is highly variant, SEQ ID NO:2 is insufficient to describe the genus ... [t]hus applicant was not in possession of the claimed genus.

See, Paper No. 02052004, at pages 11-13. Applicants respectfully disagree and traverse this rejection.

Again, Applicants respectfully point out that claims 12 and 13 have been cancelled without prejudice or disclaimer, thereby obviating the present rejection.

Applicants further respectfully point out that pending claims 23-54 do not encompass variant polypeptides. Accordingly, Applicants respectfully request that the Examiner reconsider and withdraw the present rejection under 35 U.S.C. § 112, first paragraph, for lack of written description.

III Rejections Under 35 U.S.C. § 102

The Examiner has rejected claims 12 and 13 under 35 U.S.C. § 102(b), as allegedly being "anticipated by McLean et al. (1990)." More specifically, the Examiner alleges that "[c]laim 12 is directed to a polypeptide comprising at least 15 amino acid residues of SEQ ID NO:2. There is no limitation wherein the amino acids of SEQ ID NO:2 must be contiguous. McLean et al. teaches the cloning and expression of a human integrin beta5 subunit (see page 17128, Figure 1), which comprises 15 amino acids of SEQ ID NO:2 (see

Sequence Comparison A, attached). Thus claim 12 is anticipated." *See*, Paper No. 02052004, at page 14. Applicants respectfully disagree and traverse this rejection.

Applicants respectfully point out that claims 12 and 13 have been cancelled without prejudice or disclaimer. Applicants further respectfully point out that pending claims 23-54 do not encompass polypeptides comprising amino acids of the invention without the limitation that said amino acids be contiguous. Therefore, the rejection has been obviated.

Accordingly, Applicants respectfully request that the Examiner reconsider and withdraw the present rejection under 35 U.S.C. § 102(b).

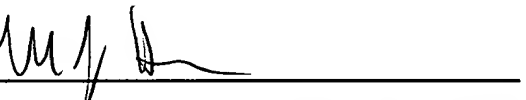
Conclusion

In view of the foregoing remarks, applicants believe that this application is now in condition for allowance. The Examiner is invited to call the undersigned at the phone number provided below if any further action by applicant would expedite the examination of this application.

Finally, if there are any fees due in connection with the filing of this paper, please charge the fees to our Deposit Account No. 08-3425. If a fee is required for an extension of time under 37 C.F.R. § 1.136 not accounted for above, such an extension is requested and the fee should also be charged to our Deposit Account.

Respectfully submitted,

Dated: May 14, 2004



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Enclosures
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